CLAIMS

What is claimed is:

1. A method of identifying polynucleic acid encoding at least one polypeptide capable of interacting, *in vivo* with a polypeptide of interest comprising;

a) contacting at least one array of plasmids with a nucleic acid probe, wherein;

i) said probe encodes the polypeptide of interest or fragment thereof, wherein said probe hybridizes to complementary sequence, if present, within any of the plasmids of the array, and wherein;

ii) said array comprises two or more plasmid partners, wherein a first plasmid partner comprises a first library fused to a first nucleic acid sequence encoding a first half of a selection pair and a second plasmid partner comprises the same or a second library fused to a second nucleic acid sequence encoding a second half of a selection pair wherein the plasmid partners are selected to be in the array by their ability to produce active selection pair in a host cell and wherein the plasmid partners are present in the array at known locations, and;

b) detecting probe hybridized to the array, thereby identifying polynucleic acid encoding at least one polypeptide capable of interacting, *in vivo*, with the polypeptide of interest.

2. The method of Claim 1, wherein the selection pair comprises a DNA binding domain and a transcriptional activation domain.

3. The method of Claim 2, wherein the DNA binding domain sequence is selected from the group consisting of: GAL, lexA, GCN4 and ADR1.

4. The method of Claim 2, wherein the transcription activation domain sequence is selected from the group consisting of: GAL, GCN4, ADR1 and herpes simplex VP16.

5. The method of Claim 1, wherein the first library is normalized.

6. The method of Claim 1, wherein the second library is normalized.

7. The method of Claim 1, wherein the library of the first plasmid partner is fused at its 5' end to the first nucleic acid sequence.

8. The method of Claim 1, wherein the library of the first plasmid partner is fused at its 3' end to the first nucleic acid sequence.

9. The method of Claim 1, wherein the library of the second plasmid partner is fused at its 3' end to the second nucleic acid sequence.

10. The method of Claim 1, wherein the library of the second plasmid partner is fused at its 5' end to the second nucleic acid sequence.

11. The method of Claim 1, wherein the plasmid partners are in separate linked arrays.

12. The method of Claim 1, wherein the plasmid partners are together in the same array.

13. The method of Claim 1, wherein the host cell is a prokaryotic cell.

14. The method of Claim 1, wherein the host cell is an eukaryotic cell.

15. The method of Claim 1, wherein a) further comprises a third plasmid comprising a sequence encoding at least one post-translational modifying enzyme.

16. The method of Claim 15, wherein the post-translational modifying enzyme is under the control of an inducible promoter system.

17. The method of Claim 15, wherein the post-translational modifying enzyme is selected from the group consisting of kinases, phosphatases, glycosylation enzymes and endoproteases.

18. The array of Claim 1, wherein the array comprises at least one set of plasmids comprising two or more plasmid partners, wherein a first plasmid partner comprises a first library fused a first nucleic acid sequence encoding a first half of a selection pair and a second plasmid partner comprising the same or a second library fused to a second nucleic acid sequence encoding a second half of a selection pair, and wherein the plasmid partners are selected to be in the array by their ability to, in concert, activate the selection pair in a host cell.

19. A method of identifying polynucleic acid encoding at least one polypeptide capable of interacting, *in vivo*, with a polypeptide of interest, wherein the interaction is affected by post-translational modification, comprising;

a) contacting at least one array with a nucleic acid probe, wherein;

i) said probe encodes the polypeptide of interest or fragment thereof, wherein said probe hybridizes to complementary sequence, if present, within any of the plasmids of the array, and wherein;

ii) said array comprises two or more plasmid partners, wherein a first plasmid partner comprises a first library fused to a first nucleic acid sequence encoding a first half of a selection pair, a second plasmid partner comprising the first or a second library fused to a nucleic acid

sequence encoding a second half of a selection pair and a third plasmid partner comprising a polynucleic acid sequence encoding at least one post- translational modifying enzyme, wherein the first and second plasmid partners are selected by their ability to produce active selection pair in a host cell in a manner dependent upon the third plasmid partner and wherein the first and second plasmid partners are present in the array at known locations; and

b) detecting probe hybridized to the array, thereby identifying polynucleic acid encoding at least one polypeptide capable of interacting, in vivo, with polypeptide of interest.

20. The method of Claim 19, wherein production of active selection pair occurs in the presence of post-translation modify enzyme encoded by the third plasmid partner.

21. The method of Claim 20, wherein the selection pair comprises a DNA binding domain and a transcriptional activation domain.

22. The method of Claim 21, wherein the DNA binding protein domain sequence is selected from the group consisting of: GAL, lexA, GCN4 and ADR1.

23. The method of Claim 21, wherein the transcription activation domain sequence is selected from the group consisting of: GAL, GCN4, ADR1 and herpes simplex VP16.

24. The method of Claim 19, wherein the first library is normalized.

25. The method of Claim 19, wherein the second library is normalized.

26. The method of Claim 19, wherein the library of the first plasmid partner is fused at its 5' end to the first nucleic acid sequence.

27. The method of Claim 19, wherein the library of the first plasmid partner is fused at its 3' end to the first nucleic acid sequence.

28. The method of Claim 19, wherein the library of the second plasmid partner is fused at its 3' end to the second nucleic acid sequence.

29. The method of Claim 19, wherein the library of the second plasmid partner is fused at its 5' end to the second nucleic acid sequence.

30. The method of Claim 19, wherein the plasmid partners are in separate linked arrays.

31. The method of Claim 19, wherein the plasmid partners are together in the same array.

32. The method of Claim 19, wherein the post-translational modifying enzyme is selected from the group consisting of: kinases, phosphatases, glycosylation enzymes and endoproteases.

33. The method of Claim 19, wherein the post-translational modifying enzyme is under the control of an inducible promoter system.

34. The method of Claim 33, wherein the inducible transcriptional system is selected from the list consisting of: MET25, heat shock, GAL and tetracycline sensitive promoters.

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35. The method of Claim 19, wherein the interaction is inhibited by the post-translational modification.

36. The array of Claim 19, wherein the array comprises at least one set of plasmids comprising two or more plasmid partners, wherein a first plasmid partner comprises a first library fused to a first nucleic acid sequence encoding a first half of a selection pair and a second plasmid partner comprising the same or a second library fused to a second nucleic acid sequence encoding a second half of a selection pair, and wherein the plasmid partners are selected to be in the array by their ability to, in concert, activate the selection pair in a host cell.

37. A composition comprising at least one array of plasmids comprising two or more plasmid partners at known locations, wherein a first plasmid partner comprises a first library fused to a first nucleic acid sequence encoding a first half of a selection pair and a second plasmid partner comprising the same or a second library fused to a second nucleic acid sequence encoding a second half of a selection pair, and wherein the plasmid partners are selected to be in the array by their ability to, in concert, activate the selection pair in a host cell.

38. A composition comprising an array of plasmids comprising two or more plasmid partners at known locations wherein a first plasmid partner comprises a first library fused to a nucleic acid encoding a DNA binding domain, a second plasmid partner comprises the first or a second library fused to a nucleic acid sequence encoding a transcriptional activation domain, wherein the first and second plasmid partners are selected to be in the array by their ability to, in concert and in the absence of expression of post-translational modifying enzyme, activate transcription of one or more marker genes in a host cell, wherein said post-translational modifying enzyme is encoded by a third plasmid partner in the host cell.

39. A composition comprising an array of plasmids comprising two or more plasmid partners at known locations wherein a first plasmid partner comprises a first library fused to a nucleic acid encoding a DNA binding domain, a second plasmid partner comprises the first or a second library fused to a nucleic acid sequence encoding a transcriptional activation domain, wherein the first and second plasmid partners are selected to be in the array by their ability to, in concert and in the presence of expression of post-translational modifying enzyme, activate transcription of one or more marker genes in a host cell, wherein said post-translational modifying enzyme is encoded by a third plasmid partner in the host cell.

40. The composition of Claim 39, wherein the selection pair comprises a DNA binding domain and a transcriptional activation domain.

41. The composition of Claim 40, wherein the DNA binding protein domain sequence is selected from the group consisting of: GAL, lexA, GCN4 and ADR1.

42. The composition of Claim 39, wherein the first library is normalized.

43. The composition of Claim 39, wherein the second library is normalized.

44. The composition of Claim 39, wherein the library of the first plasmid partner is fused at its 5' end to the first nucleic acid sequence.

45. The composition of Claim 39, wherein the transcription activation domain sequence is selected from the group consisting of: GAL, GCN4, ADR1 and herpes simplex VP16.

46. The composition of Claim 39, wherein the library of the first plasmid partner is fused at its 3' end to the first nucleic acid sequence.

47. The composition of Claim 39, wherein the library of the second plasmid partner is fused at its 3' end to the second nucleic acid sequence.

48. The composition of Claim 39, wherein the library of the second plasmid partner is fused at its 5' end to the second nucleic sequence.

49. The composition of Claim 39, wherein the plasmid partners are in separate linked arrays.

50. The composition of Claim 39, wherein the plasmid partners are together in the same array.

51. The composition of Claim 39, wherein the post-translational modifying enzyme is selected from the group consisting of kinases, phosphatases, glycosylation enzymes and endoproteases.

52. The composition of Claim 39, wherein the post-translational modifying enzyme is under the control of an inducible promoter.

53. The composition of Claim 52, wherein the inducible promoter is selected from the list consisting of: MET25, heat shock, GAL and tetracycline sensitive promoters.

54. A kit comprising at least one array of plasmids comprising two or more plasmid partners at known locations, wherein a first plasmid partner comprises a first library fused to a first nucleic acid sequence encoding a first half of a selection pair and a second plasmid partner comprising the same or a second library fused to a second nucleic acid sequence encoding a second half of a selection pair, and wherein the plasmid partners are selected to be in the array by their ability to, in

concert, activate the selection pair in a host cell and buffers for hybridizing polynucleic acids of interest to said array, and instructions for hybridization.

55. A method of generating an array of plasmids comprising;

a) conducting a two-hybrid screen, wherein a bait plasmid comprises a cDNA library and a prey plasmid comprises the same or a second cDNA library;

b) selecting positive two-hybrid clones and;

c) immobilizing the bait and prey plasmids from said positive clones on a solid support at known locations, thereby generating an array of plasmids.